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A SORE THROAT EPIDEMIC OF UNUSUAL TYPE

INFLUENZA STUDIES. VIII.

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An unusual disorder involving the upper respiratory tract was observed among the students of the High and Elementary Schools of the University of Chicago during March, 1920, and continued more or less in evidence for the following three months. The condition was noted by the school physician, Dr. Monilaw, to whom we are indebted for valuable assistance in connection with routine throat examinations, first in grades 3 A and 3 B (children 9 to 10 years old), subsequently in grade 2 B (6 to 7 years), in grade 7 B (12 to 13 years) and in many high school students. Subjective symptoms were slight although some of the children at times reported slightly sore or irritated throats with a general loss of ambition. The teachers noticed that during March the younger children were below par physically and less bright than usual. The school quarter was nearing its end, however, and such observations are not infrequent at that time.

Objectively, the children had sometimes a general lassitude, often a degree or two of fever, usually a mild but distinct reddening, more persistent and pronounced than in the average throat, of tonsillar pillars, soft palate, uvula or pharynx and occasionally enlargement of the cervical lymph nodes. In no instance were the tonsils intensely inflamed. The most striking clinical feature and the one which led to our study of what appeared to be an epidemic was the extension of redness along the tonsillar pillars toward the uvula. This redness about the tonsillar region, together with the fact noted in our early laboratory tests that the bacterial growth in material from the tonsils was more abundant than in that from the pharynx, suggested that we were dealing with an unusual chronic tonsillitis, although many of the children gave a history of tonsillectomy.

The Respiratory Disease Commission was asked to investigate grade 2 B from which 9 children were selected for intensive study. This

study was extended and to a certain degree controlled by examination of 7 children from grade 3 B in which conditions had been observed similar to those found in grade 2 B, of 7 children from grades 5 and 6 in which conditions were thought to be normal and of 8 high school students who were convalescent from sore throats of a different clinical character than that just described.

Our work with grade 2 B was started on March 17 (1920) and observations were made for 3 consecutive days before the spring vacation (March 20 to April 2) intervened. After the return of the children to school weekly or biweekly examinations were conducted until the close of the spring quarter about the middle of June. A final observation was made after the children resumed their school work in the autumn.

The number of examinations made, together with the laboratory designation of each subject and the location in school was as follows: In Grade 2 B (intensively studied): E 1, 2; E 2, 9; E 3, 10; E 4, 11; E 5, 10; E 6, 7; E 7, 9; E 8, 10; E 9, 9; in Grade 3 B (probably involved in the epidemic): E 25, 1; E 26, 1; E 27, 1; E 28, 1; E 29, 1; E 30, 1; E 31, 1; in Grade 5 A-B (probably normal): E 21, 1; E 22, 1; E 23, 1; E 24, 1; in Grade 6 A-B (probably normal): E 18, 1; E 19, 1; E 20, 1; in high school (sore throat convalescents): E 10, 1; E 11, 1; E 12, 1; E 13, 1; E 14, 1; E 15, 1; E 16, 1; E 17, 1.

The clinical symptoms tended to persist as first observed among the children of grade 2 B. Elevated temperature was found in all cases at least once, in subject E 4 nine times in 11 observations, in E 5 nine in 10 observations, in E 6 six in 7 and in E 8 eight in 10. Redness of the pharynx and tonsillar pillars was continuously observed in this group for one month and in four subjects for 12 weeks. Redness of the uvula was found only in the early examinations. The children in grade 3 B, with the exception of subject E 31 to be described later, were free from any marked symptoms except slight temperature elevations. Those in grades 5 A-B and 6 A-B were normal in all respects. On the other hand, the high school students (sore throat convalescents) showed in all instances a distinct redness of the pharynx accompanied in 4 subjects by tonsillar redness and a slight temperature elevation.

Epidemiology.—In any elementary school there is opportunity for more or less intermingling of children from all classes both inside the school and at play. Conditions, therefore, exist for the spread of respiratory infections. The laboratory data obtained in this study furnished further evidence, although not conclusive, of such inter-

mingling. The records of both the high and elementary schools showed that there were more absences than usual during the month of April (1920) on account of "sore throats," "pharyngitis" and "tonsillitis" and that throat infections were unusually prevalent during the entire spring quarter (April 2 to June 10).

There were also indications of a connection between high school students and those in the elementary grades. For example, W.P., a high school student, was the brother of J.P., a child in grade 2 B. About April 10 W.P. developed a sore throat much more severe than that prevalent among the younger children, though also atypical in character. On returning to school (April 21) hemolytic streptococci and type 4 pneumococci belonging to the same biologic groups as those present in the throats of the children in grade 2 B were isolated from his throat. The mother of W.P. and J.P. and a sister and brother home from another college for the holidays also had an infection giving, as did that of W.P., the following clinical picture: a sore throat which their family physician found unusual and unlike follicular tonsillitis, difficulty in swallowing, a temperature of 102 F. and in two cases accompanied by a rash.¹ Hemolytic streptococci were found in the throats of 5 others in the high school group and type 4 pneumococci in 3, but the biologic grouping of these organisms was not determined in all cases.

Laboratory Studies.—The clinical observations were accompanied each time by laboratory studies on the bacterial flora of the tonsillar region. Swabs were made from the tonsils and streaked on blood-agar plates in the usual manner. The swabs were then placed in 5% sheep blood dextrose broth and incubated 6-8 hours. One c.c. of the blood broth culture was then injected into a white mouse. If the animal died within 24 hours the peritoneal cavity was washed and the presence or absence of fixed type pneumococci determined by agglutination and precipitin tests. Cultures were made on blood-agar plates from the peritoneal fluid and heart blood and the usual confirmatory tests made for pneumococci. The blood-agar plates made from the original tonsillar swabs were incubated for 24 hours and then studied in the usual manner.

The first examination of cases E 1 to E 9, made on March 17, 1920, showed the presence of a hemolytic streptococcus on all plates and of a type 4 pneumococcus in all instances. These two organisms were the

¹ Scarlet fever was considered as a possibility but the symptoms did not warrant such a diagnosis.

principal ones sought for in subsequent examinations of all subjects, those serving as controls as well as those having pathologic throats. Table 1 gives the number of times these organisms were found in comparison to the attempts made in the selected group from grade 2 B.

TABLE 1
HEMOLYTIC STREPTOCOCCI AND PNEUMOCOCCI IN GROUP 2 B

Case	Number of Examinations for Streptococci	Number of Times Hemolytic Streptococci Found	Percentage Positive	Number of Examinations for Pneumococci	Number of Times Type 4 Pneumococci Found	Percentage Positive
E1	2	2	100	2	2	100
E2	9	5	56	6	5	83
E3	11	8	73	5	4	80
E4	12	11	92	7	4	57
E5	12	9	75	5	4	80
E6	7	4	57	4	4	100
E7	9	7	78	6	6	100
E8	9	7	78	6	5	83
E9	9	6	67	7	5	71
Totals.....	80	59	...	48	39	
Average.....	74	81

The laboratory examinations show that hemolytic streptococci were isolated in 74% of attempts made and type 4 pneumococci in 81%.

The control group, including 8 convalescents from sore throat, gave hemolytic streptococci in 9 instances (41%) and type 4 pneumococci in 10 instances (45%). Eight of the 9 strains of hemolytic streptococci and 4 of the 10 strains of pneumococci were isolated from the group of convalescents.

TABLE 2
AGGLUTINATION OF HEMOLYTIC STREPTOCOCCI

Strain	Serum 4 (5) TH1 Dilutions					Serum 7 (8) TH1 Dilutions				
	1:160	1:320	1:640	1:1,280	1:2,560	1:80	1:160	1:320	1:640	1:1,280
1 TH 1	+	+	+	+	+	+	+	—	—	—
4 (5) TH 1	+	+	+	+	+	+	+	—	—	—
4 (5) TH 2	+	+	+	+	+	+	+	+	—	—
4 (5) TH 5	+	+	+	+	—	+	+	—	—	—
4 (6) TH 5	+	+	+	+	+	+	+	—	—	—
7 (5) TH 1	+	+	+	+	+	+	+	+	—	—
7 (6) TH 1	+	+	+	+	+	+	+	+	+	—
12 TH 2	+	+	+	+	+	+	+	+	—	—
17 TH 2	+	+	+	+	+	+	—	—	—	—

The hemolytic streptococci found on the blood plates were difficult to grow on transfers made to blood-agar slants. We were able to obtain them only from subjects E 1, E 4, E 7, E 12, E 14, and E 17. All strains from E 1, E 4, E 7, E 12 and E 14 fermented lactose, mannite and salicin, thus falling in Holman's group *S. infrequens*. Strains

from E 17 did not ferment mannite. Immune serums for 2 strains [4(5)TH 1 and 7(6)TH 1] were prepared by injection of rabbits and agglutination tests made against a number of strains with the results recorded in table 2.

Three strains from influenza cases gave no agglutination in any dilution with either serum. The strains from case E 1 was isolated at the first examination. Three strains from case E 4 were obtained 3 weeks after the first observation and one strain after 4 weeks. The two strains from case E 7 were isolated after 3 and 4 weeks, respectively. The strains isolated were thus biologically identical, including the strain from subject E 17 which was culturally different.

The type 4 pneumococci were likewise tested with an immune serum prepared with one of the strains (E 4-6). Table 3 gives the results of agglutination.

TABLE 3
AGGLUTINATION OF TYPE 4 PNEUMOCOCCI

Strain	Dilutions (Serum E 4-6)								
	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	1:2,560
E 2-5	+	+	+	+	+	+	+	+	+
E 2-7	+	+	+	+	+	+	—	—	—
E 3-5	+	+	+	+	+	—	—	—	—
E 3-6	+	+	+	+	+	—	—	—	—
E 4-6	+	+	+	+	+	+	+	+	+
E 5-5	+	+	+	+	—	—	—	—	—
E 5-6	+	+	+	—	—	—	—	—	—
E 6-3	+	+	+	+	+	—	—	—	—
E 8-5	+	+	+	+	—	—	—	—	—
E 9-4	+	+	+	+	+	—	—	—	—
E 10	+	+	+	+	+	—	—	—	—
E 12	+	+	+	+	—	—	—	—	—
E 15	+	+	+	—	—	—	—	—	—
E 16	—	—	—	—	—	—	—	—	—
E 24	—	—	—	—	—	—	—	—	—
E 27	+	+	+	—	—	—	—	—	—
E 31	+	+	+	+	+	+	+	—	—

Strains from cases of common colds gave no agglutination with this serum. As with the hemolytic streptococci the strains were obtained at various times—from 2 days to 4 weeks after our work was started. A biologically identical type 4 pneumococcus was thus isolated from all the cases of grade 2 B except 2 from which the strains failed to survive, from 3 high school students and from 2 children of grade 3 B.

The persistence of clinical symptoms in some cases led to a study of the length of time that hemolytic streptococci and type 4 pneumococci remained in the throats of the children of grade 2 B. Unfortunately it was not possible to complete this part of the investigation because of the withdrawal from school of some of the children and

the closing of school for the summer. Table 4 gives the available data correlated with the appearance of tonsils and pharynx.

These results show a close correlation between clinical observations and the presence of hemolytic streptococci, pneumococci or both.

An examination made October 25, after the autumn opening of the school, revealed the persistence of clinical symptoms in group 2 B. These, however, were less severe in character than those noted 7 months previously. Hemolytic streptococci were absent from all throats while type 4 pneumococci were isolated in 2 instances. It is not known that these 2 strains were identical with those previously studied.

TABLE 4
PERSISTENCE OF HEMOLYTIC STREPTOCOCCI AND PNEUMOCOCCI (PRESENCE AFTER 8 WEEKS)

Subject	Redness of Pharynx	Redness of Tonsils	Hemolytic Streptococci	Type 4 Pneumococci
E 2	+	Slight	+	+
E 3	0	Doubtful	+	+
E 4	+	+	+	+
E 5	+	+	+	—
E 6	0	0	—	+
E 7	+	0	—	+
E 8	0	0	—	—
E 9	0	0	+	—

* Numbers very few.

Subject E 31, a member of grade 3 B, proved to be of some interest. This child had an attack about June 9 and presented a clinical picture of a more severe character than observed in the other children. The pharynx became so acutely inflamed, edematous and painful that the head was retracted. The temperature rose several degrees. We isolated from the tonsils a type 4 pneumococcus serologically identical with the others studied but failed to find a hemolytic streptococcus. Whether or not the pneumococcus was the etiologic factor is unknown, but the finding of a specific serum strain of this organism in connection with a distinct pathologic condition is worth noting.

SUMMARY

The data here presented show the occurrence of a sore throat epidemic of an unusual clinical type. A hemolytic streptococcus and a type 4 pneumococcus were found simultaneously in the tonsillar regions of a group of children with the symptoms described. The streptococcus was of an unusual cultural type, belonging to Holman's group S. infrequens. The hemolytic streptococcus is known to be at times the etiologic factor in sore throats. That the type 4 pneumo-

coccus present in our group might be pathogenic is suggested by its presence unaccompanied by hemolytic streptococci in one case of acute inflammation.

One of the most striking features was the carrier condition. It is impossible to say how long this was maintained, but in 5 of 8 instances it persisted for not less than 8 weeks as shown by finding immunologically identical organisms continually on the tonsils during this period. Hemolytic streptococci were found after 12 weeks. The proportion of hemolytic streptococci in the tonsillar flora as indicated on blood-agar plates varied considerably, some examinations being negative. It is well recognized that the technic usually employed may yield discrepancies. The reappearance of these organisms on blood-agar plates does not necessarily mean that a new invasion has occurred. We had no way of determining the relative numbers of the pneumococcus.

The finding of specific strains of hemolytic streptococci and of type 4 pneumococci, biologically identical with those from the group of children intensively studied, in convalescents among high school students and in children in other grades of the elementary school indicated the prevalence of these organisms throughout the whole school. The possibility of contact among the children existed and was substantiated by certain well established instances.

The persistence of clinical symptoms closely paralleled the occurrence of the two specific strains of the organisms (see table 4). These symptoms were so mild after the earliest examinations as almost to escape attention.

This epidemic may have been caused by one of the organisms isolated or by their simultaneous action.